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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,685	07/28/2003	Ann H. Cornell-Bell	2314-268	4593

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,685	CORNELL-BELL ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

HC

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of the κ-PVIIA peptide having an amino acid sequence set forth in SEQ ID NO:26 in the amendment and response to restriction requirement filed January 13, 2005 is acknowledged, and two new claims 20 and 21 have been added. The traversal is on the ground(s) that all the peptides claimed which are either a generic formula (SEQ ID NO:1) or analogs of PVIIA having specific sequences (SEQ ID NOs:2-26), all peptides are related to a single peptide, κ-PVIIA, and have the same activity, namely treating disorders associated with radical depolarization of excitable membranes by activating a K_{ATP} channel; and there are limited numbers of peptides in the Markush group, thus, search and examination of the entire claim can be made without much burden. The argument is found persuasive (pages 12-15 of the response), thus, the restriction requirement is withdrawn and claims 1-21 with SEQ ID NOs: 1-26 are examined.

Informalities

2. The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (page 7, line 15). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code from this page of the application and to review and appropriately amend by deletion any other instances of browser executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating hypoxia-induced depolarization or glutamate-induced excitotoxicity *in vitro* using kappa-conotoxin PVIIA (κ-PVIIA), does not reasonably provide enablement for a method for treating a disorder associated with radical depolarization of excitable membranes, such as cardiac ischemia, cerebral ischemia, asthma or ocular ischemia *in vivo* by administering a κ-PVIIA peptide (e.g., SEQ ID NOs:1-26 or a derivative thereof). The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-21 encompass a method for treating disorders associated with radical depolarization of excitable membranes (Claims 1-4, 9, 20), cardiac ischemia (claim 5, 10-19, 21), cerebral ischemia (claim 6), asthma (claim 7) or ocular ischemia (claim 8) *in vivo* by administering a κ-PVIIA peptide (e.g., SEQ ID NOs:1-26 or a derivative thereof). The specification, however, only discloses cursory conclusions (pages 4-6) without data supporting the findings, which state kappa-conotoxin PVIIA peptides, analogs and derivatives are used for activating ATP-sensitive K^+ channels and the opening of ATP-sensitive K^+ channels is useful for treating many disorders such as cardiac ischemia, cerebral ischemia, asthma and ocular ischemia. There are no indicia that the present application enables the full scope in view of treating a disorder associated with radical depolarization of excitable membranes by administering a κ-

PVIIA peptide (e.g., SEQ ID NOs:1-26 or a derivative thereof). The present application does not provide sufficient teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the derivatives of SEQ ID NO:1, the treating condition for a specific disorder such as cardiac ischemia, cerebral ischemia, asthma and ocular ischemia, and the effects of the conotoxins in the treatment, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no working examples indicating the claimed methods in association with the variants except for the data that κ-PVIIA produces dose-dependent hyperpolarization, has protective effect against hypoxia induced depolarization *in vitro*, and is effective as a bronchodilator *in vitro* (Examples 4, 7, 8 10 and 11).

(3). The state of the prior art and relative skill of those in the art:

The related art (references indicated at pages 17-19 of the specification) shows that K^+ channels openers are effective relaxants of airway smooth muscle reducing hyperactivity induced obstruction of intact airway, and they have beneficial vasodilatory effects in patients with angina

pectoris and show great promise as cardioprotective agents. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the treating condition for a specific disorder associated with radical depolarization of excitable membranes and the effect of the κ-PVIIA peptide in the treatment of the disorders for to be considered enabling for variants.

(4). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method for treating disorders associated with radical depolarization of excitable membranes such as cardiac ischemia, cerebral ischemia, asthma or ocular ischemia in an individual by administering a κ-PVIIA peptide (e.g., SEQ ID NOs: 1-26 or a derivative thereof). The specification indicates κ-PVIIA produces dose-dependent hyperpolarization, has protective effect against hypoxia induced depolarization *in vitro*, and is effective as a bronchodilator *in vitro* (Examples 4, 7, 8 10 and 11), however the specification does not demonstrate the use of κ-PVIIA or derivatives thereof in treating disorders associated with radical depolarization of excitable membranes *in vivo*, nor indicating the effect of the conotoxin peptide in the treatment. Moreover, there are no examples indicating the *in vivo* treatment, and the specification has not shown how to extrapolate the in vitro data to in vivo effect. Although the general treating conditions such as the dosage of the conotoxin peptide has been cited in the specification (pages 14-16), the treating condition for a specific disorder such as cardiac ischemia, cerebral ischemia, asthma or ocular ischemia and the in vivo effect of the κ-PVIIA peptide on the disease is not shown. Since the specification fails to provide sufficient guidance on the treatment for a specific disorder associated with radical depolarization of

excitable membranes using the κ- conotoxin PVIIA peptide, it is necessary to have additional guidance and to carry out undue experimentation to assess the effect of the conotoxin peptide.

(5). Predictability or unpredictability of the art:

The claims encompass treating disorder associated with radical depolarization of excitable membranes, however, the treating condition for a specific disorder and the effect of the κ-PVIIA peptide are not sufficiently described in the specification, the invention is highly unpredictable regarding the outcome of the treatment.

(6). Nature of the Invention

Scope of the claims includes treating disorder associated with radical depolarization of excitable membranes, but the specification does not indicate how various disorders are treated using the κ-PVIIA peptide, nor demonstrates the effect of theκ-PVIIA peptide in the treatment. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed methods, and the guidance and the teaching in the specification are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the outcome of the treatment using the conotoxin peptide. Thus, practice of the full scope of the presently claimed invention based upon the current claims requires the practice of undue experimentation.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-10, 12, 14, 16, 18, 20 and 21 are indefinite because they lack an essential step in the process of treating disorders. The omitted step is the outcome of the treatment. Claims 2-9, 12, 14, 16, 18, 20 and 21 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

6. Claims 1-19 are indefinite because of the use of the term "a derivative of (a) or (b)". The term "a derivative of (a) or (b)" renders the claim indefinite, it is not clear what structure the derivative has, and how different the derivative is from the parent compound. Claims 2-9 and 11-19 are included in the rejection because they are dependent on rejected claims and do not correct the deficiency of the claim from which they depend.

7. Claims 9 and 18 are indefinite for because of the use of the term "may be substituted", "may be glycosylated", "may be". The term "may be substituted", "may be glycosylated", "may be" or "may be replaced" renders the claim indefinite, it is unclear whether the substitution, glycosylation or replacement occurs or not as to "may be". One interpretation of this type of language is that none of the modifications are present or some or all are present but is unclear because the above are representative of alternative interpretations of the claims. Claims 9 and 18 are also indefinite because of the use of the term "derivatives", it is not clear what structure the derivative has, and how different the derivative is from the parent compound. Regarding claims

9 and 18, the phrase "e.g." renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

8. Claim 11 recites the limitation "the size of reperfusion infarct" in line 1. There is insufficient antecedent basis for this limitation in the claim. See also claims 13, 15, 17 and 19.

Conclusion

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8700.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner

CHIH-MIN KAM
PATENT EXAMINER

CMK
April 25, 2005